UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,482	12/12/2005	Frans Eduard Janssens	PRD2077f-PCT-USA	3160

27777 7590 06/13/2008

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
4161	

MAIL DATE	DELIVERY MODE
06/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,482	JANSSENS ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/29/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *9 and 21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claim

Claims 15-20 have been cancelled and new claims 21-26 have been added. Claims 1-14 and 21-26 are currently pending.

Election/Restrictions

Applicants' election of group I drawn to a composition and election of the following species: (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as a specific species from the generic chemical structure of formula (I) compound and fentanyl as one species from the different opioid analgesics, in the reply filed on May 29, 2008, are acknowledged. The above election was made with traverse. The traversal is on the ground that the claimed compositions reduce to a large extent the unwanted side-effects associated with opioid analgesics and there is no undue search burden since the search for each Group would be essentially the same. This is not found to be persuasive because of the following reasons: the composition which is the common technical feature for both groups is shown in the prior art disclosing their effects on reducing the unwanted side-effects associated with opioid analgesics, therefore groups I and II do not related to a single general inventive concept under PCT Rule 13.1 due to their lack of the same or corresponding special technical features under PCT Rule 13.2. In addition, search burden being undue is a moot argument for lack of unity issue. Undue search burden is not an issue in a lack of unity. The requirement is still deemed proper and is therefore made final.

Claims 9 and 21-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1-8 and 10-14 are under examination in the instant office action.

Priority

The instant application is a 371 of PCT/EP04/11548 filed on 6/7/2004 and claims benefit of foreign application filed on 6/10/2003. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). A certified copy of foreign application has been submitted on 12/12/2005.

The earliest effective U.S. filing date afforded the instantly claimed invention has been determined to be 6/7/2004.

Information Disclosure Statement

Information disclosure statement has not been filed.

Claim Objections

Claim 8 is objected because of the following informalities: typographical errors. Claim 8 not ending with a period should be corrected.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 11-14 and are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claims contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

a) The quantity of experimentation necessary: Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed compound, for example, is in fact a prodrug, that produces the active compound metabolically in man at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

b) The amount of direction or guidance presented: The direction concerning the prodrugs is found in the instant specification (p11, line 32-p12, line 18).

c) The presence or absence of working examples: There is no working example of a prodrug of a compound represented by the formula (I).

d) The nature of the invention: The nature of the invention is clinical use of the compounds and the pharmacokinetic behavior of substances in the human body.

e) The state of the prior art: Wolff (Medicinal Chemistry) summarizes the state of the prodrug art (Wolff, Manfred E. "Burger's Medicinal Chemistry, 5ed, Part I", John Wiley & Sons, 1995, pages 975-977). The table on the left side on page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker et al. in the first sentence of third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug (Banker et al, "Modern Pharmaceutics, 3ed.", Marcel Dekker, New York, 1996, pages 451 and 596).

f) The relative skill of those in that art: Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience.

g) The predictability or unpredictability of the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

h) The breadth of the claims: The instant claims include hundreds of thousands of compounds of formula (I) as recited in claim 1 as well as the presently unknown list of potential prodrug derivatives embraced by claim 1.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

1) Claims 1-8, and 10-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/25988 (publication date: 7/24/1997) in view of US patent 6,197,772 B1 (issue date: 3/6/2001).

The instant invention is drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier, an opioid analgesic (elected species: fentanyl), and 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives represented by formula (I) (elected species: (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid). In other embodiments, the composition is formulated for simultaneous, separate or sequential use (claim 11) and is orally administered (claim 14).

WO 97/25988 teaches a pharmaceutical composition comprising a compound with tachykinin antagonist activity including NK_1 receptor antagonist activity and non-tachykinin receptor antagonist analgesic including fentanyl, together with at least one pharmaceutically acceptable carrier, diluents or excipient for the treatment or prevention of pain or nociception (abstract; p7, 1st paragrph; p31, last paragraph; p32; and p44, 1st compound). WO 97/25988 further teaches that the composition can be administered by a variety of routes including oral, rectal, transdermal, subcutaneous, intravenous, intramuscular, and intranasal (p48, 1st paragraph) and the administration of the non-tachykinin receptor antagonist analgesic may be simultaneous

with, before, or after the administration of the tachykinin receptor antagonist (p58, 5th paragraph). These teachings read on limitations recited in the instant claims 11 and 14. In addition, WO 97/25988 discloses that the combination therapy is advantageous because a marked decreased amount of a traditional analgesic can be administered, which would lessen the likelihood and severity of any adverse effects (p47, 2nd paragraph). The reference differs from the instant claims insofar as it does not teach 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives recited in claim 1 including the elected species, (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid.

US patent 6,197,772 B1 teaches the same generic chemical structure of 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives represented by formula (I) and (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as a preferable embodiment as recited in the instant claims 1 and 10 (column 1, line 44-column 4, line 23; column 7, line 39-column 8, line 5; claims 1-3). In addition, US patent 6,197,772 B1 teaches that 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives have tachykinin antagonistic activity, in particular substance P (NK_1 receptor agonist) antagonistic activity (column 1, lines 9-14) and can be used for the treatment of pain, emesis, or asthma (column 18, lines 33-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO 97/25988 with the teachings of US patent 6,197,772 B1 for the treatment of pain and/or nociception because of the following reasons: according to WO 97/25988, the pharmaceutical composition comprising a NK_1 receptor

antagonist and a non-tachykinin receptor antagonist analgesic such as fentanly is effective on the treatment or prevention of pain or nociception and possible side effects of other analgesics. US patent 6,197,772 B1 teaches (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as NK_1 receptor antagonist. Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to be motivated to substitute one NK_1 receptor antagonist in the prior art with another NK_1 receptor antagonist such as (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid for the combination with a opioid analgesic in order to provide the same effect.

2) Claims 1-8, and 10-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US patent 5,880,132 (issue date: 3/9/1999) in view of US patent 6,197,772 B1.

US patent 5,880,132 teaches a pharmaceutical composition comprising a tachykinin antagonist in paricular an NK_1 receptor antagonist and an opoid analgesic, together with at least one pharmaceutically acceptable carrier or excipient for the treatment or prevention of pain or nociception (abstract; column 1, lines 7-10; and column 2, lines 33-36). US patent 5,880,132 defines that the term opioid is generally accepted to refer in a generic sense to all drugs, natural or systhetic with morphone-like action (column 1, line 52-56), which encompasses fentanyl. US patent 5,880,132 further teaches that the composition may be present as a combined preparation for simultaneous, separate or sequential use for the treatment or prevention of pain (column 2, lines 42-46 and claim 4). This teaching reads on the limitations recited in instant claim 11. In addition, US patent 5,880,132 discloses that the composition is possible to treat pain with a sub-

maximal dose of an opioid analgesic thereby reducing the likelihood of side-effects associated with opioid analgesic usage such as nausea, vomiting, and tolerance. The reference differs from the instant claims insofar as it does not teach 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives recited in claim 1 including the elected species, (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid.

US patent 6,197,772 B1 teaches the same generic chemical structure of 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives represented by formula (I) and (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as a preferable embodiment as recited in the instant claims 1 and 10 (column 1, line 44-column 4, line 23; column 7, line 39-column 8, line 5; claims 1-3). In addition, US patent 6,197,772 B1 teaches that 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives have tachykinin antagonistic activity, in particular substance P (NK_1 receptor agonist) antagonistic activity (column 1, lines 9-14) and can be used for the treatment of pain, emesis, or asthma (column 18, lines 33-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patent 5,880,132 with the teachings of US patent 6,197,772 B1 for the treatment of pain and/or nociception because of the following reasons: according to US patent 5,880,132, the pharmaceutical composition comprising NK_1 receptor antagonist and an opoid analgesic is effective on the treatment or prevention of pain or nociception and possible side effects of opoid analgesics. US patent 6,197,772 B1 teaches a (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-

dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as NK_1 receptor antagonist. Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to be motivated to substitute one NK_1 receptor antagonist in the prior art with another NK_1 receptor antagonist in the instant invention for the combination with a opioid analgesic in order to provide the same effect.

3) Claims 1-8, and 10-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US patent application publication 2002/0052504 (publication date: 5/2/2002) in view of US patent 6,197,772 B1.

US patent application publication 2002/0052504 teaches a pharmaceutical composition comprising a piperidine derivative having a potent NK_1 receptor antagonist activity in combination with other analgesics such as opioid anangegics inlcuding fentanyl, together with at least one pharmaceutically acceptable carrier or excipient for the treatment or prevention of pain or nociception ([0002], [0076] and [0077]). US patent application publication 2002/0052504 further teaches the composition as a combined preparation for simultaneous or separate, or sequential use in the treatment or prevention of pain or nociception ([0078]). This teaching read on the instant claim 11. The reference differs from the instant claims insofar as it does not teach 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives recited in claim 1 including the elected species, (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid).

US patent 6,197,772 B1 teaches the same generic chemical structure of 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives represented by formula (I) and

(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as a preferable embodiment as recited in the instant claims 1 and 10 (column 1, line 44-column 4, line 23; column 7, line 39-column 8, line 5; claims 1-3). In addition, US patent 6,197,772 B1 teaches that 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives have tachykinin antagonistic activity, in particular substance P (NK_1 receptor agonist) antagonistic activity (column 1, lines 9-14) and can be used for the treatment of pain, emesis, or asthma (column 18, lines 33-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patent application publication 2002/0052504 with the teachings of US patent 6,197,772 B1 for the treatment of pain and/or nociception because of the following reasons: US patent application publication 2002/0052504 teaches the pharmaceutical composition comprising a NK_1 receptor antagonist and an analgesic such as fentanyl is effective on the treatment or prevention of pain or nociception. US patent 6,197,772 B1 teaches (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N-(2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as NK_1 receptor antagonist. Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to be motivated to substitute one NK_1 receptor antagonist in the prior art with another NK_1 receptor antagonist such as (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid for the combination with a opioid analgesic in order to get the same effect.

4) Claims 1-8, and 10-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US patent 6,136,824 (issue date: 10/24/2000) in view of US patent 6,197,772 B1.

US patent 6,136,824 teaches a pharmaceutical composition comprising a piperidine-propan-2-derivative having a potent NK_1 receptor antagonist activity in combination with other analgesics such as opioid analgesics inlcuding fentanyl, together with at least one pharmaceutically acceptable carrier or excipient for the treatment or prevention of pain or nociception (column 1, line 63-column 2, line 2 and column 11, line 4-34). US patent 6,136,824 further teaches the composition as a combined preparation for simultaneous or separate, or sequential use in the treatment or prevention of pain or nociception (column 11, line 35-39). This teaching read on the instant claim 11. The reference differs from the instant claims insofar as it does not teach 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives recited in claim 1 including the elected species, (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid).

US patent 6,197,772 B1 teaches the same generic chemical structure of 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives represented by formula (I) and (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as a preferable embodiment as recited in the instant claims 1 and 10 (column 1, line 44-column 4, line 23; column 7, line 39-column 8, line 5; claims 1-3). In addition, US patent 6,197,772 B1 teaches that 1-(1, 2-disubstituted piperidinyl)-4-substituted piperazine derivatives have tachykinin antagonistic activity, in particular substance P (NK_1 receptor agonist) antagonistic activity (column 1, lines 9-14) and can be used for the treatment of pain, emesis, or asthma (column 18, lines 33-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patent 6,136,824 with the teachings of US patent 6,197,772 B1 for the treatment of pain and/or nociception because of the following reasons: US patent 6,136,824 teaches the pharmaceutical composition comprising a NK_1 receptor antagonist and an analgesic such as fentanly is effective on the treatment or prevention of pain or nociception. US patent 6,197,772 B1 teaches (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as NK_1 receptor antagonist. Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to be motivated to substitute one NK_1 receptor antagonist in the prior art with another NK_1 receptor antagonist such as (B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid for the combination with a opioid analgesic in order to provide the same effect.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 8:00-5:00 Monday-Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BONG-SOOK BAEK
Examiner, Art Unit 4161

Bbs

/Ashwin Mehta/

Primary Examiner, Technology Center 1600